Proposed Biology of Development and Aging Integrated Review Group

Summary of Public Comments

The Biology of Development and Aging (BDA) Study Section Boundaries Team met July 15-17, 2001, to design the study sections of the proposed BDA Integrated Review Group (IRG) and draft proposed guidelines. These guidelines were made available for public comment on the Center for Scientific Review (CSR) Web site for a 12-week period that ended in November 2001. CSR also received correspondence concerning the organization of this IRG.

In examining these comments, one should note that the study section guidelines created by the Study Section Boundaries Teams are recommendations to CSR. For recommendations to go forward they must be consistent with CSR policies and practices. For example, some have found that the BDA guidelines recommend moving areas of behavioral science and epidemiology to BDA. While movement to BDA may be consistent with a current trend toward integrative approaches, it would be premature. At this time, CSR and the Panel on Scientific Boundaries for Review are committed to no substantial changes in the neuroscience and behavioral science IRGs pending stabilization after their recent reorganization and formal evaluation. Thus, the BDA study sections to be formed will not be handling behavioral, epidemiology, and nursing applications at their outset.

Comments received are summarized below. General comments on this proposed IRG are presented first, followed by comments related to the structure or content of specific study sections and the expertise needed for them to function effectively.

General Comments

Aging Community

CSR received several comments expressing a clear interest in aging aspects of the BDA guidelines. Collectively they seem to represent a strong endorsement from the aging research community.

1. ***Impact on Aging Research:*** Some perceive that no appropriate study sections for biology of aging grant applications currently exist. As a result, these applications often go to study sections lacking aging expertise and are often streamlined excessively. Representatives of several aging organizations and other commenters were pleased with the proposed IRG and believed that it would not only address current perceptions of problems but usher in a new era of productive, rigorous research that will have profound implications for understanding of these basic processes. They were particularly pleased with the proposed Aging Systems and Geriatrics (ASG) Study Section, which will cover age and physiology, geriatric syndromes, and multifactor problems with an aging focus.

2. ***Range of Study Sections:*** A view was that the proposed guidelines reflect a sophisticated understanding of the integrated disciplines necessary to fully elucidate mechanisms of both development and aging. Members of the aging community approved of the two aging-related study sections: Cellular Mechanisms of Aging and Development (CMAD) and ASG, which cover translational research spanning basic and clinical aspects. These individuals also supported the Panel on Scientific Boundaries for Review principle of flexible reviews, which calls for study sections to have some overlap so that an application can be reviewed in more than one venue.

3. ***Valuable Aspects of the New Guidelines:*** Favorable comments were received on linking review of organogenesis, differentiation, metamorphosis, and animal cloning in the Developmental 1 Study Section (DEV-1); including the signaling in the context of development (DEV-1); and clustering morphogenesis, epithelial-mesenchymal transitions and cell-polarity in DEV-2.

4. ***Responsive and Integrative Approach:*** The descriptions of the proposed CMAD and ASG study sections seem to be highly responsive to the needs of the aging community, which strongly supports the creation of these new study sections. Community members were particularly pleased that the proposed ASG study section would ensure that there would be at least one appropriate study section for reviewing applications with an integrated research approach to studying the challenging health problems of older adults. They noted that interdisciplinary research will be key to making progress in challenging areas of geriatrics research and that ASG is demonstrative of such efforts.

Reproductive Sciences Community

Comments were received from multiple members of the reproductive sciences community. Several expressed concern about aspects of reproductive sciences in BDA:

1. ***Division of Reproductive Research:*** Multiple members of the reproductive sciences community voiced concern over the potential division of their discipline between two IRGs: BDA and Endocrinology, Metabolism and Reproductive Sciences. Thus, the new BDA study sections may dilute the importance of and marginalize the area of reproductive sciences and lessen focus on fertility and population issues. Grant applications on reproductive processes may be reviewed by scientists who lack expertise or enthusiasm for reproductive research or who do not even have a minimal background in the field. In turn, reproductive scientists expressed discomfort with reviewing proposals in organogenesis, metamorphosis, or regeneration. The BDA proposal as a whole may have a negative impact upon the science. Under the proposal, it will be difficult to distinguish the areas of the science that may be appropriate for a particular IRG and those that would be better served by remaining with reproduction and endocrinology. Others suggested that consideration of gametogenesis and fertilization would be incomplete without the context of gamete transport and storage in the male and female reproductive tracts. Creating

reproductive biology study sections in BDA may be duplicative, repetitive, and likely to create tensions and conflicts.

2. ***Society for the Study of Reproduction Proposal:*** Support was expressed for a proposal by the Society for the Study of Reproduction to divide the Endocrinology, Metabolism and Reproductive Sciences IRG into two IRGs. An Endocrinology and Metabolism IRG would cover endocrinology, metabolism, and nutrition via current or revised study sections:
(1) Endocrinology, (2) Metabolism, and (3) Nutrition. The second IRG would be called Reproductive Sciences and encompass all of the reproductive sciences research currently reviewed in the (1) Reproductive Biology, (2) Human Embryology and Development 1, (3) Reproductive Endocrinology, (4) Biochemical Endocrinology. The boundaries of these study sections could remain the same or be revised. Some suggested a need for additional input from the reproductive science community.

3. ***Placement of Reproductive Science Research:*** Some were disturbed that reproductive science subjects from gametogenesis through placental developmental, early embryogenesis, and animal cloning are considered in a study section that deals with far-ranging aspects of development. While the logic of considering some aspects of gametogenesis and even early embryogenesis along with other basic topics of development is understood, the inclusion of this broad area of reproductive sciences in such a setting may be problematic.

4. ***Gonadal Research:*** Gonadal biologists may consider their work more endocrine in nature than developmental and prefer to have their applications reviewed by peers in that group. Some believe that elements of gametogenesis and gonadal biology would be more properly combined with the rest of reproduction, endocrinology, and perhaps nutrition, as it is becoming more endocrinology oriented. Other topics such as gastrulation and pattern formation certainly seem easily separated from reproductive biology.

5. ***Endometrial and Endocrine Research***: As to the impact on reproductive endocrinology/ implantation studies, embryologists and those who study development models will not be able to review adequately endometrial or endocrine-related grant applications. Reproductive biologists working on the maternal side may not be given a fair review under the proposed guidelines.

6. ***Human Embryology and Development Research:*** Concerning the impact on the Human Embryology and Development 1 (HED-1) Study Section, one of the strengths of the reorganization should be the ability to bring together experts whose perspectives contribute to a more comprehensive review and evaluation of research topics. The current HED-1 study section already has a strong multidisciplinary character, since it addresses pregnancy, reproduction issues, fetal and neonatal diseases/development; and contains expertise in the areas of obstetrics, perinatology, fetal physiology and development, neonatology, infant development, etc. Reviewers in this study section understand how their field of expertise is affected by research in other fields because

of the close interrelations of the medical and scientific questions. While the proposed BDA is intended to do the same, it may actually dilute this multidisciplinary strength.

7. ***Scope of the Developmental 1 Study Section:*** Some doubt exists about the ability of the DEV-1 study section to garner the expertise necessary to review the divergent pool of applications assigned to it. Imprinting and animal cloning can fall within the expertise of DEV-1. Gametogenesis, germ/somatic interactions, fertilization, implantation, and placental development belong in a more focused group.

8. ***Gametogenesis and Organogenesis Research:*** Another opinion was that having gametogenesis reviewed in the same section as organogenesis would trivialize the differences between them.

9. ***Other Areas of Reproductive Research:*** A concern is that other areas of reproductive sciences could be misplaced in other IRGs such as Renal and Urological Sciences or the Molecular Approaches to Cell Function and Interactions IRGs.

10. ***Comparative Biology:*** There was a question as to where comparative biology (e.g., work on large farm species) lies.

Social Sciences, Nursing Research, and Epidemiology Communities

The social sciences, nursing research, and epidemiology communities expressed concern that the BDA proposal may change the homes of many of the research areas established under the social sciences reorganization. Common themes among the comments are provided below:

1. ***Reviewing Epidemiology Studies:*** Some expressed the view that these studies are unique and require the special review of epidemiologists and behavioral scientists. Basic scientists often do not understand or appreciate epidemiology. In addition, epidemiologic studies are often costly, so basic scientists often review them harshly. The current system of assigning epidemiology grant applications related to aging to an epidemiology study section is the right way to do these reviews.

2. ***Appreciating the Methods of Social Science Research:*** One epidemiologist, who explores social behavioral linkages with biological relationships, uses methods that are social science in origin. Also, an approach of large population natural research also follows a more social science model rather than a classical biomedical or even narrow epidemiological model. A fear is that the proposed BDA would tend to be the review locus for applications on social behavioral exploration of aging biological issues (e.g., diet, activity, and sarcopenia), which may harm the field.

3. ***Addressing Priorities for Social Science Research:*** One view was that the organization of BDA unfortunately might create a social science underclass in the review process that is counter the mandate of Congress (and its understanding of what is currently important, for example, the failure of translational research to reach

populations). It is also counter to the new Institute of Medicine report on Health Behavior, 2001, which urges much better applied social science research.

4. ***Giving ASG a Focus on Research Methodology:*** Another view was that the Social Science, Nursing, Epidemiology and Methods 3 (SNEM-3) Study Section consists of demographers, many of whom are actively involved in research on the issue of longevity and on the patterns/predictors of mortality and morbidity among human beings. How the ASG areas of interest will be differentiated from SNEM-3's is unclear. ASG should be distinguished from other IRGs by its methodology, not by the "endpoints" of the aging process.

5. ***Assessing Special Issues:*** An Epidemiology and Diseases Control 1 (EDC-1) Study Section member emphasizes the need to scrutinize the many special issues that arise in this area of research, such as issues of study design, biostatistical methods, logistics of population-based studies, and the potential for biases in this research. Attempting to integrate these types of studies into the more biological work reviewed by BDA may reduce the quality of the reviews and thus the quality of the research funded. Although funding in this area may not diminish, the quality of research may suffer because of reduced success in identifying the most promising proposals.

6. ***Assessing the Multifactoral Etiology of Disease:*** One person recommended that the Epidemiology and Diseases Control (EDC) study sections be preserved in their current format and with current types of members to ensure appropriate scientific review. The projects reviewed by the EDC study sections were described as among the most complex and important anywhere, as these projects attempt to understand better the multifactor etiology of human diseases and their sequelae.

7. ***Reviewing Nursing Research:*** Applications from nurse researchers that directly or indirectly address clinical nursing practice issues must continue to be assigned to the Nursing Research Study Section to allow appropriate and effective review of these proposals. If such applications go to BDA, the potential exists for a grave reduction in the development of evidence-based nursing practices and new nursing knowledge throughout the United States at a critical time in nursing. The Nursing Research Study Section is not included on the list of Shared Interests for BDA.

8. ***Importance of Nursing Expertise:*** An opinion was that nursing research and ASG overlaps include, but are not limited to, musculoskeletal problems and geriatric syndromes and behavioral interventions. A study section with knowledge and expertise in clinical issues is best able to review those types of clinical studies.

9. ***Importance of Behavioral Expertise:*** A researcher studying sexual diseases reports sometimes serving as a behavioral scientist ambassador on review groups dominated by clinical and biological scientists. One of the severe weaknesses of many clinically based studies is the poor measurement of behavior. This weakness is attributable to the lack of behavioral expertise in the clinical and biological community. This individual

thus urges reconsideration of the BDA guidelines that seem to set up again review groups lacking sufficient depth and weight from behavioral science disciplines.

10. ***Value of Social Science Review Groups:*** Several comments reflected a desire for greater sensitivity to the important contributions social and behavioral sciences make to NIH extramural research programs and for greater recognition of the value of social science review groups. Furthermore, some thought that forming study sections with only one or two social/behavioral scientists would lead to reviews dominated by biological scientists and result in a decrease in the variety and depth of socio-behavioral research supported by NIH. On the other hand, some stated that social and behavioral scientists should be included in the disease and organ-related IRG where the potential for significant shared interests exists.

Comments on Specific Study Sections

Aging Systems and Geriatrics (ASG) Study Section

1. ***Large Areas of Overlap:*** Some comments expressed concern for the large overlap with existing study sections, particularly those with mandates to review social and behavioral projects. In addition, overlap may exist between ASG and the Integrative, Functional and Cognitive Neuroscience 5 Study Section in the area of postural control and balance. When strong shared interests do occur, expert and fair review requires that appropriate and representative social scientists, biologists, and clinical scientists be involved.

2. ***Wide Range of Topics:*** There is a concern that selection of reviewers with the expertise needed to address the wide range of topics in ASG will be difficult.

3. ***Definition of "Disability":*** One view was that the term "disability" must be included in the ASG guidelines. Under "geriatric syndromes," the term "loss of functional independence" is used. Scientists working in the area of aging and disability recognize the risk of confusing "loss of function" with the more global problem of disability.

4. ***Separating Alzheimer's Disease and Late-Life Dementias:*** Another view was that a perhaps unrealistic and artificial distinction seems apparent: applications specifically related to Alzheimer's disease should be reviewed in the Brain Disorders and Clinical Neuroscience IRG, while applications related to late-life dementias, including but not limited to Alzheimer's disease, would go to ASG.

Cellular Mechanisms in Aging and Development (CMAD) Study Section

1. ***Definition of "Embryonic Cell Cycles":*** Regarding the inclusion of "embryonic" in the fourth bullet under CMAD, the meaning of "embryonic cell cycles" is unclear.

2. ***Placement of Embryonic and Fetal Topics:*** As to the fifth bullet that includes "embryonic, fetal" in addition to "adult", those topics could be included in DEV-1 or -2 to leave CMAD strictly for aging applications.

3. ***Placement of Cell-Matrix Communication:*** Grant applications encompassing the more general principles of cell-matrix communication could also be reviewed by CMAD.

DEV-1 and DEV-2 Study Sections

1. ***Overlooked Area:*** Programming due to external agents and/or the maternal environment has been overlooked.

2. ***Role of Maternal Tissues:*** Listed under DEV-1 emphasis is pre-implantation, implantation, and placental development. Concern exists that this is a narrow view, which suggests that implantation is solely controlled by gametes and embryos. Reviewers must be chosen who appreciate the importance of maternal tissues during the developmental process.

3. ***Clustering of Topics:*** Concern exists with the breadth of topics and choices based upon study section composition. One suggestion is to add additional developmental study sections that have narrower scopes (e.g., more on the scale of DEV-1 without the regeneration topic). All of the clinically related topics such as regeneration, birth defects, and stem cells could be clustered into a third study section. If there are fewer topics covered in each study section, the total number of reviewers might not have to increase.

4. ***Clustering of Cell Fate with Stem Cells:*** Cell fate and stem cells (both in DEV-2) might have extensive overlap, in particular in consideration of the overall goals of the research, to topics of organogenesis and differentiation (covered in DEV-1). Another commenter suggested that clustering cell fate and stem cells with cell biological processes of polarity and migration (all now in DEV-2) seems less ideal since fundamentally different questions will likely be encountered. This also is a reason for shifting cell fate and stem cell research to DEV-1.

5. ***Placement of Signaling:*** Signaling could be in DEV-1, in DEV-2, or outside of the IRG, depending on the application or context of the experiments, so assignment of applications should be flexible.

6. ***Decreased Importance of Cell Lineage:*** Among areas of review, the significance of cell lineage is now diminished as discussion has moved beyond "cell lineage" as a primary principle. It should not appear as a separate topic.

7. ***Merging Gametogenesis and Organogenesis*** into one study section (DEV-1) seems odd.

8. ***Placement of Mesodermal Organs:*** Under the description of organogenesis, why mesodermal organs (such as the kidney and spleen) were left out is unclear. The lung is an endodermal organ, and may not merit a separate listing. Why epithelial-mesenchymal transitions (an integral part of organogenesis) are separated is questioned.

9. ***Placement of Nervous System Development:*** Objection was expressed about moving the nervous system developmental biology from the Molecular, Cellular and Developmental Neuroscience IRG study sections.

10. ***Use of the Term "Apoptosis":*** NIH should consider using the term "programmed cell death" rather than "apoptosis" as apoptosis is likely to be only one pathway of programmed death.

11. ***Placement of Human Disorders:*** Ambiguity exists about where human disorders such as recurrent abortion are reviewed.

12. ***Having a Multidisciplinary Approach:*** Requests were made for a reconsideration of the decision to specify particular subject specialties for the proposed DEV-1 and DEV-2 study sections. NIH may receive the best value for its investment if both study sections review the full spectrum of developmental applications. This is more in keeping with the increasingly multidisciplinary approach of modern and high quality developmental biology.

Other Comments

1. ***Fundamental Cell Biological Processes:*** One opinion was that a potential disadvantage may exist for those studying fundamental cell biological processes related to development including cell cycle and death. Their proposals could be assigned to different study sections.

2. ***Genetic Factors:*** Another opinion was that emphasis should be given to understanding genetic factors that are involved in development and aging, and to taking advantage of the magnificent resources generated by the Human Genome Project.

3. ***Kinetics and Differentiation of Adult Somatic Tissue Cells:*** A different opinion was that the proposed study sections do not attend to research that addresses adult somatic tissue cell kinetics and differentiation with a systems approach. Much of the expertise is designed for reductionist approaches that fail to consider the integrated kinetics and differentiation architecture of adult tissues.

4. ***Developmental Pharmacology:*** A study section with expertise in human developmental biology related to drug action, drug metabolism, and effects of xenobiotics on the developmental organism are advocated. Currently, there is no home for these proposals.

5. ***Importance of Cognate Disciplines:*** Some welcome peer review groups that combine solid expertise in relevant cognate disciplines with an appreciation for key issues in aging and geriatric medicine. The division of CMAD (with its cellular orientation) and ASG (with its emphasis on integrative pathophysiology and whole animal models) makes sense.

6. ***Importance of Whole Animal Studies:*** One commented that the use of whole animal studies should be included to test hypotheses that might be derived from cellular, biochemical, and/or molecular studies.

7. ***Alternate Vertebrate and Invertebrate Systems:*** The BDA guidelines should clarify if alternative vertebrate and invertebrate systems will get serious consideration, and some attempt should be made to include individuals with expertise outside the usual models and systems on review groups. More specifically, sex differentiation and development is not mentioned but is subsumed under (a) organogenesis, (b) differentiation, and (c) signaling.

8. ***Dispersement of ECM/Cell Adhesion Applications:*** A member of the ECM/cell adhesion field is concerned that excessive scattering of grant applications addressing basic ECM/cell adhesion biology occur due to splitting of these topics into their "applied" categories. This will leave these grant applications as minorities in study sections with too few members that have credible expertise in ECM/cell adhesion to adequately assess their scientific merits.

9. ***Stem Cell and Developmental Biology:*** One view was that growth is expected in these areas. As in the National Institute of Diabetes and Digestive and Kidney Diseases, attention should be given to developmental genetic screens; signaling pathways; and transcription factors that regulate pattern formation and control cell fate, as well as cell specification and proliferation/differentiation of bone, adipose, pancreas, and pituitary.

10. ***Clustering of Cell/Death and Apoptosis Grants:*** As to the disposition of cell death/apoptosis grant applications, the Cell Development and Function 5 study section has been reviewing grants on the basic mechanisms of apoptosis, whether they have to do with development, neuronal function, or carcinogenesis. Some see as appropriate that this group of grant applications should continue to be compared with each other when judging scientific merits.

Acronyms

ASG	Aging Systems and Geriatrics Study Section
BDA	Biology of Development and Aging
CMAD	Cellular Mechanisms of Aging and Development
CSR	Center for Scientific Review
DEV-1	Developmental 1 Study Section
DEV-2	Developmental 2 Study Section
EDC-1	Epidemiology and Diseases Control 1
HED-1	Human Embryology and Development 1 Study Section
IRG	Integrated Review Group
NIH	National Institutes of Health
SNEM-3	Social Science, Nursing, Epidemiology and Methods 3 Study Section